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RESEARCH ARTICLE

Computer-Based *versus* Paper-Based Insulin Infusion Algorithms in Diabetic Ketoacidosis

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Abstract: ***Background*:** Paper-based and computer-based insulin infusion algorithms facilitate appropriate glycemic therapy. The data comparing these algorithms in the management of diabetic ketoacidosis in the intensive care unit (ICU) setting are limited. We aimed to determine the differences in time to diabetic ketoacidosis resolution and incidence of hypoglycemia between computer and paper-based insulin infusion.

***Methods*:** Single-institution retrospective review of patients admitted to the ICU with diabetic ketoacidosis between 4/1/2015 and 7/20/2018. Our institution introduced computer-based insulin infusion (Glucommander) to the intensive care unit on 3/28/2016. Patients were grouped into either paper-based group (preintervention) or a computer-based group (postintervention). Summary and univariate analyses were performed.

***Results*:** A total of 620 patients (paper-based=247; computer-based=373) with a median (IQR) age of 40 (26-56) years were included; 46% were male. Patients in the computer-based group were significantly older (p=0.003); otherwise, there were no significant differences in gender, race, body mass index and HbA1c. The mean (±SD) time to diabetic ketoacidosis resolution in the computer-based group was significantly lower than the paper-based group (p=0.02). The number of patients in the paper-based group who developed severe hypoglycemia (<50 mg/dl) was significantly higher {8% vs 1%; p<0.0001}.

***Conclusion*:** Our analyses demonstrate statistically significant decreases in time to DKA resolution and hypoglycemic events in DKA patients who were managed using a computer-based insulin infusion algorithm providing a more effective and safer option when compared to paper-based insulin infusion.

Keywords: Diabetic ketoacidosis, insulin, glucommander, hypoglycemia, algorithm, diabetes.

1. INTRODUCTION

The complexity of insulin infusion management in hyperglycemic disorders necessitates a systematic approach that facilitates safe practices and reduces the risk of errors [1]. Paper-based insulin infusion algorithms and computer-based insulin infusion algorithms are useful tools for facilitating appropriate glycemic therapy [2]. These algorithms allow for predefined adjustments in the insulin infusion rate based on glycemic fluctuations. Glucommander (GM), one example of a computer-based insulin infusion that is commonly used in the management of diabetic ketoacidosis (DKA), originated from an article published in 1982 by White *et al*. and is a personalized evidence-based system that advises on intravenous (IV) insulin dosing by using multivariate algorithms [3-5]. The software continuously recalculates the insulin dose and dynamically adjusts to each individual patient's sensitivities and other clinical variables, such as patient height, weight, blood glucose (BG), hemoglobin A1c (HbA1c) and carbohydrate consumption. It also gives recommendations on how frequently glucose levels must be checked. GM is typically implemented and executed on a computer where a physician specifies the initial parameters, including target glucose and the multiplier or insulin sensitivity factor. The nurse caring for the patient enters the appropriate parameters and the point-of-care glucose. GM then recommends an insulin infusion rate and a time to check the next BG. This process continues until the ordering physician discontinues the algorithm.

Computer-based insulin infusion is advertised as superior to paper-based insulin infusion in managing DKA as it minimizes human-related errors. However, to our knowledge, there are very limited data comparing paper-based insulin infusion with computer-based insulin infusion in the management of DKA in the intensive care unit (ICU) setting. Thus, whether computer-based insulin infusion is superior to paper-based insulin infusion in the management of DKA is unknown. In the present study, we sought to explore the differences between computer-based insulin infusion and paper-based insulin infusion for the following outcomes: time to

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DKA resolution, time to targeted glucose reading, incidence of hypoglycemic events, length of ICU and length of hospital (LOS) stay. We hypothesize that the time to DKA resolution is shorter with computer-based insulin infusion use than with paper-based insulin infusion use.

2. MATERIALS AND METHODS

Institutional review board approval was obtained, and a single-institution retrospective analysis was performed for patients admitted with DKA between 4/1/2015 and 7/20/2018. Our institution transitioned from paper-based insulin infusion to computer-based insulin infusion in March 2016 using GM to facilitate insulin dosing. Our institution comprises two hospitals; a University affiliated hospital and a community hospital. We introduced GM to all seven of our health system's ICUs. The intravenous GM software licensed by Glytec was used, and the multiplier used at our institution is 0.01. This multiplier has been selected based on previous evidence suggesting improved treatment outcomes when selecting a multiplier of 0.01 in the management of DKA [6]. The GM software is installed on computers in the ICU only. The GM software continuously recalculates the insulin dose and dynamically adjusts to each individual patient's sensitivities. It then automatically adjusts the insulin infusion and gives recommendations on how frequently glucose levels must be checked. The paper-based insulin infusion algorithm used at our institution was created by endocrinologists at our facility using the American Diabetes Association (ADA) guideline as a reference (Supportive/Supplementary Material) [7]. When using our paper-based insulin infusion, nurses start patients on a fixed insulin infusion rate of 0.1 U/kg/hour and based on the subsequent BG readings or rate of BG drop, further adjustments in the insulin infusion rate are manually performed by the nurse.

Adult (>18 age) patients with either type 1 or type 2 diabetes mellitus were included in the study if they met DKA criteria on admission, were admitted to the ICU directly from the emergency department and were treated with insulin infusion within four hours of arrival to the emergency department. The IV insulin used in our insulin infusion protocols is regular insulin. DKA diagnostic criteria included hyperglycemia (glucose>250 mg/dl), acidosis (bicarbonate level <18 mEq/l) and ketosis (ketones in urine or blood) [7]. The following patients were excluded from the study: 1) <18 years of age, 2) did not meet criteria for DKA diagnosis, 3) diagnosed with diabetic hyperosmolar hyperglycemic state, 4) admitted to the medical ward, 5) patients with more than four hours delay in insulin infusion initiation or 6) treated with subcutaneous insulin. The patients were subsequently divided into two groups. The paper-based group includes patients admitted prior to 3/28/2016 and the computer-based group includes patients admitted after 3/28/2016 who were managed using the GM.

Demographic data were collected. Time and date at the following points were recorded: admission, insulin infusion initiation, insulin infusion discontinuation, first BG <250 mg/dl (13.9 mmol/L) and first anion gap (AG) ≤17. At our institution, basic metabolic panels are checked every 4 hours. Point-of-care BG levels were checked hourly in the paper-based group, while timing for BG checks was determined by GM in the computer-based group. Time to insulin infusion initiation was defined as insulin infusion initiation time minus emergency department arrival time. Time on insulin infusion is the total time on insulin infusion and was defined as insulin infusion discontinuation time minus insulin infusion initiation time. Time to DKA resolution was defined as the time of first AG ≤17 minus insulin infusion initiation time. The upper limit of the normal AG at our institution is 17. The time to target glucose was defined as the time of first BG <250 mg/dl (13.9 mmol/L) minus insulin infusion initiation time. A target BG of less than 250 mg/dl (13.9 mmol/L) was set as IV fluids transition to dextrose 5% ½ normal saline when BG <250 mg/dl (13.9 mmol/L). Moreover, the discontinuation of insulin drip was based on clinician judgments; thus, any unnecessary excessive time on insulin infusion was defined as insulin infusion discontinuation time minus time of first AG <17. Hypoglycemic events were reported only during time on insulin infusion. Given the short half-life of intravenous insulin, hypoglycemic events that occurred after the discontinuation of insulin infusion were not included. Hypoglycemia was categorized as mild (<80 mg/dl) or severe (<50 mg/dl). The incidence and severity of hypoglycemic events were recorded for each patient. Further, bicarbonate level on admission, ICU model (open vs closed), BG level on admission (prior to initiation of insulin), inpatient mortality, LOS, ICU stay and HbA1c level were recorded. Only HbA1c levels within 6 months of admission were recorded. If there were multiple HbA1c levels within the suggested timeframe, the closest value to the admission date was recorded. The primary outcome was time to DKA resolution. Secondary outcomes included time to insulin infusion initiation, time on insulin infusion, time to target glucose, unnecessary excessive time on insulin infusion, incidence of mild and severe hypoglycemia, number of hypoglycemic events per patient, inpatient mortality, hospital LOS and ICU stay. All data were abstracted from the electronic medical record (EPIC). We designed a report to extract the aforementioned data points. Following automated extraction, the data was randomly validated by three reviewers (MY, MH, HA). There were no discrepancies identified.

Normally distributed continuous variables were reported as means ±standard deviation (SD), nonparametric data were reported as medians with interquartile range (IQR), and categorical variables were reported as counts and percentages. Chi-square tests were used to compare categorical variables between the two groups, and Student's t-test was used to compare the continuous outcomes between the two groups for uniformly distributed variables. When data were not distributed uniformly, the Wilcoxon rank-sum test was used to compare the outcomes between the two groups. Multiple linear regression was performed for time to DKA resolution. Logistic regression was performed for mild and severe hypoglycemia. Post hoc power analyses were performed for the following outcomes: 1) time to DKA resolution, 2) mild hypoglycemia and 3) ICU stay. All tests were two-sided with an α level set at 0.05 for statistical significance. Data analysis was performed using JMP Pro version 10.0 (SAS Institute Inc., Cary, NC, USA).

Post hoc power analyses were performed for the following outcomes: (1) time to DKA resolution, (2) mild hypoglycemia and (3) ICU stay. Comparing the computer-based

group to the paper-based group, we demonstrated a significant 42-minute difference in time to DKA resolution with p=0.02 in 620 patients, and this result indicated that the power of this test was 64% and that the minimal detectable difference was 36 minutes and required a minimal sample size of 440 patients. We demonstrated a 42% significant reduction in mild hypoglycemia in the computer-based group compared to the paper-based group, suggesting that this test has a power of 100% and would require a sample size of 83 patients to detect a difference of 15%. We also demonstrated a significant reduction in the ICU stay by 4 hours in the computer-based group compared to the paper-based group, which estimates the power of this test to be 80% and to detect a similar difference of 3.4 hours would require 302 patients.

3. RESULTS

A total of 620 patients with a median (IQR) age of 40 (26-56) years were included; 46% (n=284) were male (Fig. **1**). Patients in the computer-based group were significantly older than patients in the paper-based group (p=0.003) (Table **1**). There were 247 (40%) patients in the paper-based group, and 373 (60%) patients in the computer-based group.

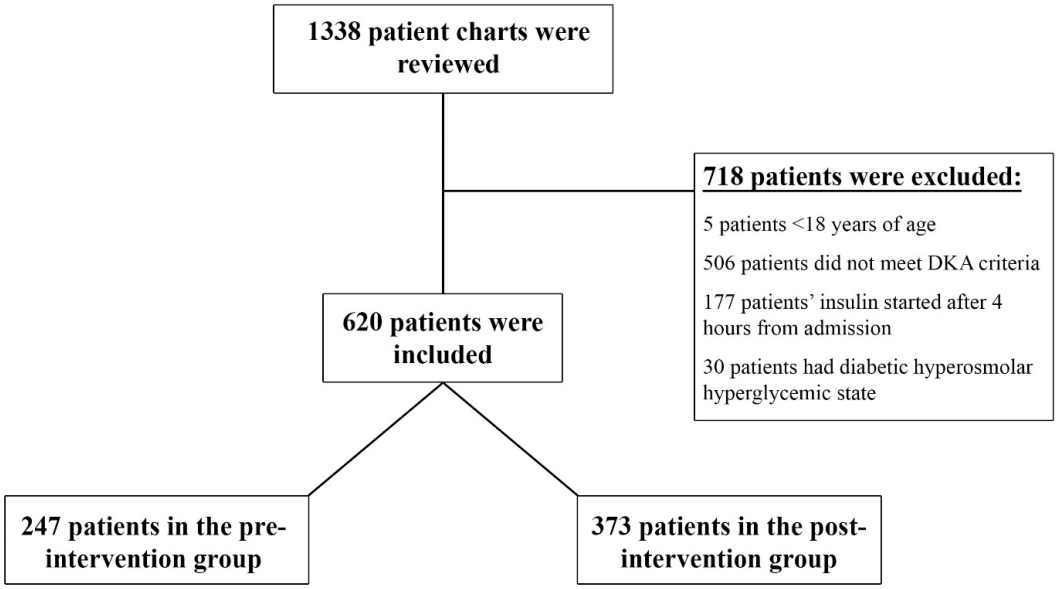

Fig. (1). Study flow diagram showing the patient population selection process.

Table 1. Patient clinical and laboratory characteristics.

Characteristic	Paper-based (n=247)	Computer-based (n=373)	p value
Age, median (IQR)	35 (25-53)	42 (29-57)	0.003*
Sex, n (%)	Male: 106 (43%) Female: 141 (57%)	Male: 178 (48%) Female: 195 (52%)	0.24
BMI, mean (±SD)	27 (7)	26 (6)	0.24
Race, n	Caucasian: 193 African American: 48 Other: 6	Caucasian: 277 African American: 81 Other: 15	0.41
Type of ICU, n (%)	Open: 237 (96%) Closed: 10 (4%)	Open: 248 (66%) Closed: 125 (34%)	<0.0001*
HbA1c, mean (±SD)	11.4 (2.4) % 101 (21) mmol/mol	11.6 (2.8) % 103 (25) mmol/mol	0.28
BG level, mean (±SD)	551 (196) mg/dl 30.6 (10.9) mmol/L	579 (198) mg/dl 32.2 (11.0) mmol/L	0.07
Bicarbonate level, median (IQR) in mEq/l	10 (7-14)	9 (5-13)	0.01*

BMI: Body mass index; HbA1c: Hemoglobin A1C; ICU: intensive care unit; BG: blood glucose.

All patients were admitted to either an open ICU (n=485, 78%) or a closed ICU (n=135, 22%), and the proportion of patients that were managed in an open ICU was significantly larger in the paper-based group than in the computer-based group (Table **1**). There were 129 (21%) African American patients, 470 (76%) Caucasian and 21 (3%) patients who were of Asian, American Indian, native Hawaiian or unknown race. The mean (±SD) BMI was 26±7, the mean (±SD) HbA1c was 11.5±2.7 % or 102±24 mmol/mol (57 missing values), and the median (IQR) bicarbonate level on admission was 10 (6-13) mEq/l. Patients in the computer-based group had significantly lower bicarbonate levels than those in the paper-based group (p=0.01) (Table **1**). The mean (±SD) BG level on admission in our patient population was 568 (±198) mg/dL or 31.6 (±11.0) mmol/L. There was no significant difference between groups in terms of BG level on admission, sex, BMI, race or HbA1c (Table **1**).

The mean (±SD) time to DKA resolution among our patient population was 6.9 (±3.8) hours. The mean (±SD) time to DKA resolution in the computer-based group was 6.6±3.7 hours, which was significantly lower than the time (7.3±4.0 hours) in the paper-based group (p=0.02). Additionally, when comparing patients who were managed in open ICUs only, the mean (±SD) time to DKA resolution was significantly lower in the computer-based group than in the paper-based group {6.5±3.9 vs 7.4±4.0; p=0.02}. However, when comparing patients who were managed in closed ICUs only, there was no significant difference in the mean (±SD) time to DKA resolution (p=0.45). Comparing patients in the computer-based group alone, there was no significant difference in the time to DKA resolution in patients who were treated in an open ICU compared with those treated in a closed ICU (p=0.73). Additionally, comparing patients in the paper-based group alone, there was no significant difference in the time to DKA resolution in patients who were treated in a closed ICU compared with those treated in an open ICU (p=0.10). A multiple linear regression was calculated to predict time to DKA resolution based on several predictors of interest. After adjusting for age, HbA1C level, ICU model, mild and severe hypoglycemia; the use of computer-based insulin infusion and the bicarbonate level on admission were both significantly associated with time to DKA resolution. For every participant that is managed using the computer-based insulin infusion, the time to DKA resolution decreased by 0.54 hours (p=0.0021). Also, for every unit of bicarbonate level increase, the time to DKA resolution decreased by 0.43 hours (p<0.0001).

The median (IQR) time to targeted glucose among the whole population was 3.3 (1.8-5.6) hours (54 missing values). Further, the median (IQR) time to targeted glucose was significantly lower in the paper-based group than in the computer-based group. The median (IQR) overall time on insulin infusion was 18 (12-25) hours. The median (IQR) overall time on insulin infusion in the computer-based group was significantly lower than the time in the paper-based group. The mean (±SD) time to insulin infusion initiation was significantly lower in the paper-based group than in the computer-based group. There was no significant difference in the median (IQR) unnecessary excessive time on insulin in hours between both groups. Table **2** presents the difference in secondary outcomes between both groups.

Hypoglycemia developed in 178 patients, or 29% of the total population, and was classified as either mild hypoglycemia (n=156, 25%) or severe hypoglycemia (n=22, 4%). The proportion of patients with mild and severe hypoglycemia was significantly higher in the paper-based group than that in the computer-based group (Table **3**). The median (IQR) number of hypoglycemic episodes was 2 (1-3) for mild hypoglycemia and 1 (1-2) for severe hypoglycemia in the whole population. The median (IQR) number of mild hypoglycemic events was significantly higher in the paper-based group. However, there was no significant difference in the median (IQR) number of severe hypoglycemic events between both groups. Table **3** presents the differences in hypoglycemic events between both groups.

Logistic regression was performed for mild and severe hypoglycemia in relation to several predictors of interest. In a univariate unadjusted analysis, the use of the computer-based insulin infusion was significantly associated with mild and severe hypoglycemia; for every patient treated with the computer-based insulin infusion, the odds of mild and severe hypoglycemia decreased by 88% {odds ratio: 0.12; CI (0.08-0.17); p<0.0001} and 90% {odds ratio: 0.10; CI (0.03-0.33); p=0.0002}respectively. The time to DKA resolution was also significantly associated with mild hypoglycemia; for every hour increase in time to DKA resolution, the odds of mild hypoglycemia decreased by 6% {odds ratio: 0.94; 95% CI

Table 2. Differences in secondary outcomes between both groups.

Characteristic	Paper-based (n=247)	Computer-based (n=373)	p value
Time to targeted glucose, median (IQR)	3.1 (1.6-4.8) hours	3.6 (1.8-6.2) hours	0.02*
Time on insulin infusion, median (IQR)	18 (13-29) hours	17 (11-24) hours	0.003*
Time to insulin infusion initiation, mean (±SD)	1.2 (±1.1) hours	2.3 (±0.8) hours	<0.0001*
Unnecessary excessive time on insulin, median (IQR)	12 (7-22) hours	11 (6-17) hours	0.14
LOS, median (IQR)	2 (2-4) days	3 (2-4) days	0.50
ICU stay, median (IQR)	38 (26-53) hours	34 (24-50) hours	0.005*
Mortality, n (%)	2 (0.81%)	3 (0.80%)	0.99

LOS: length of hospital stay; ICU: intensive care unit.

Table 3. Differences in the hypoglycemic events between both groups.

Characteristic	Paper-based (n=247)	Computer-based (n=373)	p value
Mild hypoglycemic events, n (%)	134 (54%)	44 (12%)	<0.0001*
Mild hypoglycemic events per patient, median (IQR)	2 (1-3)	1 (1-2)	0.0004
Severe hypoglycemic events, n (%)	19 (8%)	3 (1%)	<0.0001*
Severe hypoglycemic events per patient, median (IQR)	1 (1-2)	1 (1-1)	0.27

(0.90-0.99); p=0.01}. However, there was no significant association between severe hypoglycemia and time to DKA resolution {odds ratio: 0.95; 95% CI (0.86-1.05); p=0.32}. For a patient admitted to a closed ICU, the odds of mild hypoglycemia decreased by 62% {odds ratio: 0.38; 95% CI (0.23-0.64); p=0.0002} but there was no significant association between severe hypoglycemia and ICU model (p=0.35). There was no significant association between hypoglycemia and age {mild hypoglycemia odds ratio: 1.00; 95% CI (0.99-1.01); p=0.47 *vs.* severe hypoglycemia odds ratio: 1.00; 95% CI (0.98-1.00); p=0.69}, BG on admission {mild hypoglycemia odds ratio: 1.00; 95% CI (1.00-1.00); p=0.80 *vs.* severe hypoglycemia odds ratio: 1.00; 95% CI (1.00-1.00); p=0.50} or HbA1c {mild hypoglycemia odds ratio: 1.05; 95% CI (0.98-1.12); p=0.18 *vs.* severe hypoglycemia odds ratio: 1.12; 95% CI (0.91-1.36); p=0.51}. After adjusting for age, HbA1c, ICU model, BG on admission and time to DKA resolution, a multivariable analysis showed that the use of the computer-based insulin infusion was associated with significantly lower odds of mild and severe hypoglycemia by 87% {odds ratio: 0.13; 95% CI (0.08-0.20); p<0.0001} and 92% odds ratio: 0.08; 95% CI (0.02-0.37); p<0.0001} respectively.

The median (IQR) hospital LOS was 3 (2-4) days. There was no significant difference in the hospital LOS in days between both groups (Table **2**). The median (IQR) ICU stay was 36 (24-50) hours, and there was a significantly higher median (IQR) ICU stay in hours in the paper-based group compared with that in the computer-based group. Only 5 of the 620 patients in our cohort died; of these, four died in the ICU, and one patient died on the floor when transferred out of the ICU. There was no significant difference in the mortality rate between both groups. Lastly, none of the patients in either group developed cerebral edema.

4. DISCUSSION

In our study, our analyses demonstrate statistically significant decreases in time to DKA resolution and hypoglycemic events in DKA patients who were managed using a computer-based insulin infusion algorithm providing a more effective and safer option when compared to paper-based insulin infusion. Our study is one of few studies comparing traditional paper-based insulin infusion algorithms with computer-based algorithms such as GM [6, 8]. Our study is the only study that studies severely morbid patients in an isolated ICU setting.

Serum bicarbonate level is one of the most important indices determining the severity of DKA [9]. Patients in the computer-based group had significantly lower serum bicarbonate levels on presentation depicting more severe DKA. Nonetheless, patients in the computer-based group had shorter times to DKA resolution and times on insulin infusion. Further, insulin infusion initiation was significantly later in the computer-based group. This highlights that the observed reduction in time to DKA resolution in the computer-based group is not attributed to earlier initiation of insulin. Echoing our results, Jagdeesh Ullal *et al*. have also demonstrated more rapid bicarbonate and BG normalization times with a significantly reduced risk of hypoglycemia in patients managed using the GM [6]. Another retrospective pediatric study, involving 22 patients, concluded that patients managed using GM achieved equally rapid glycemic control and correction of acidosis, used less intravenous insulin, and spent less time in both the ICU and hospital overall compared to those managed with manual insulin infusion [8]. To our knowledge, there are no other available studies comparing the GM or computer-based insulin infusion with paper-based insulin infusion in DKA patients. There are, however, other retrospective studies comparing computer-based insulin infusion with traditional paper-based insulin infusion in non-DKA patients. These have also demonstrated comparable glucose control and a reduction in the number of severe hypoglycemic events in critically ill patients [10-11] and noncritically ill patients [12]. Likewise, we present a significant reduction in ICU stay. We also present a clinically and statistically significant reduction in hypoglycemic events in the computer-based group.

The use of GM in the computer-based group reduces the risk of nonadherence. In contrast, paper-based insulin infusion has had various outcomes at different institutions. One retrospective case review study conducted in the United Kingdom revealed that, though providers were aware of the existence of a universal protocol, this awareness did not translate into protocol adherence for several reasons, including patient- and clinician-related factors [13]. Other studies have also demonstrated suboptimal care because of low adherence stemming from discontinuity of medical care, understaffing, and less experience caring for DKA patients [14-15].

Subcategorizing our patient population based on the type of ICU they were managed in; a statistically significant reduction in time to DKA resolution was observed in patients managed using the computer-based insulin infusion in an open ICU but not in a closed ICU. Only 135 patients (22%) of our patient population were managed in closed ICUs; 10 were in the paper-based group, and 125 were in the computer-based group. Hence, we were underpowered to detect a difference in time to DKA resolution in this subgroup. Fur-

ther, more intense staffing and monitoring in closed ICUs improves adherence to medical protocols such as paper-based insulin infusion [16-17], indicating that there might be more room for improvement in the management of DKA in open ICUs than in closed ICUs. However, after controlling for confounding variables, such as the ICU model; our study consistently demonstrates a significant reduction in the time to DKA resolution when using computer-based insulin infusion.

A primary concern with DKA management and insulin infusion protocols is hypoglycemia. A large retrospective study involving 2665 patients concluded that there was a significantly lower risk of hypoglycemia in patients managed using computer-based insulin infusion compared with paper-based insulin infusion [6]. In the present study, despite a similar baseline BG level on admission, we mirrored their results demonstrating a significantly lower number of patients with mild and severe hypoglycemia in patients managed using GM. Further, the median (IQR) number of mild hypoglycemic events per patient was also significantly lower in patients managed using the GM than in those that were not. However, there was no significant difference in the median (IQR) number of severe hypoglycemic events per patient between both groups. This can potentially be explained by the very low incidence (4%) of severe hypoglycemia in our patient population. The time to target glucose levels was significantly lower in the paper-based group despite the longer time to DKA resolution. Decreased time to insulin initiation in the paper-based group is potentially a contributing factor to this observed decreased time to target glucose. The delay in insulin initiation in the computer-based group can be attributed to transition of care from the emergency department to the ICU where the GM is initiated. The clinical significance of these findings is to be doubted, though they can explain the higher rates of hypoglycemia in the paper-based group as shorter time to target glucose ultimately leads to a rapid sharp decrease in BG levels in contrast with a slow steady decrease in BG levels in the computer-based group. In both univariate and multivariate logistic regression, the odds of mild hypoglycemia significantly decreased in patients that were managed using the GM. Further, odds of mild but not severe hypoglycemia decreased when patients were managed in a closed ICU. Accumulating evidence has indicated that the quality of care in ICUs and patient outcomes are influenced by the structure and organization of ICUs [16]. Studies have consistently demonstrated that compared to a low-intensity staffing structure ("open" ICUs without a mandatory intensivist consult), high-intensity staffing (mandatory intensivist consultation or "closed" ICUs with intensivist staffing) improves outcomes [17]. Resolving any discrepancies, after adjusting for the ICU model in our multivariate logistic regression, the observed association between closed ICUs and reduction in hypoglycemia was no longer significant.

6. LIMITATIONS

We acknowledge certain limitations of this study. The time to DKA resolution was defined as the time of first AG<17 minus insulin infusion initiation time. The calculated time is therefore dependent on a laboratory value. The DKA might have resolved before the laboratory value was drawn or even resulted. Therefore, some degree of inaccuracy might ensue. However, at our institution, basic metabolic panels are drawn at a fairly tight interval of every four hours for all DKA patients admitted to the ICU. Second, patients in the computer-based group were significantly older and had lower bicarbonate levels compared to the paper-based group. Despite that, these patients still had lower time to DKA resolution and less hypoglycemic events. Also, taking the patients' other baseline characteristics such as sex, race, HbA1c and BG levels on admission into consideration would most likely minimize variation and reduce heterogeneity. Third, the patients included in the study were managed in seven different ICUs at our institution. The DKA protocols are the same across all ICUs, and their use is mandatory; however, the ICUs were either open, closed or an open ICU that transitioned to a closed ICU. One could assume that patients managed in a closed ICU had closer monitoring and therefore optimum management of DKA with a lower risk of hypoglycemia [16-17]. Since there was a significantly higher percentage of patients in the paper-based group that were managed in an open ICU, subgroup and multivariate analyses were performed to isolate any differences in outcomes in patients treated in an open ICU vs a closed ICU. Fourth, the focus of this study was limited to insulin therapy in the management of DKA. Other variables that have an impact on DKA resolution, such as fluid resuscitation and electrolyte replacement therapy, were not adjusted for in this study. Lastly, as a single institutional review in a Midwestern state, our results may not be externally valid and should be validated in multi-institutional studies to demonstrate their generalizability. However, the seven ICUs included varied between academic and community, urban and rural, and large and small, which increase the external validity of our study.

CONCLUSION

Our study demonstrates that in DKA patients, when compared with paper-based insulin infusion, the computer-based insulin infusion resulted in a statistically significant decrease in various outcomes, such as time to DKA resolution, time on insulin infusion, ICU stay and hypoglycemia. This finding suggests that the use of the computer-based insulin infusion using GM can be both safe and effective. These benefits were observed more readily in open ICUs than in closed ICUs. Our study is one of few studies comparing traditional paper-based insulin infusion algorithms with computer-based algorithms such as GM, and further multi-institutional prospective studies are essential to validate this practice.

AUTHOR CONTRIBUTIONS

Study design was developed by MY, MH, HA and JP. Data generation was performed by MH, HA and JP. Data analysis and interpretation were performed by MY and MH. Manuscript writing and editing were performed by MY, MH, JP and HA.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

IRB approval was sought prior to initiation of this study. Informed consent is not applicable given the retrospective nature of the study.

HUMAN AND ANIMAL RIGHTS

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

FUNDING

None.

CONFLICT OF INTERESTS:

Glucommander™ is a commercial product licensed by Glytec. Dr. Moustafa Younis and the other authors did not receive any honoraria, grants, or other forms of payment to produce the manuscript.

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